Heterologous production and characterization of albicidin, a potent DNA gyrase inhibitor

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Albicidin is a toxin and an antibiotic produced by the slow-growing bacterium *Xanthomonas albilineans*, the causal agent of sugarcane leaf scald. Albicidin is involved in the pathogenicity of *X. albilineans* and inhibits the replication of chloroplastic DNA. It also inhibits DNA replication in *Escherichia coli* at nanomolar concentrations, whereas mammalian cells are unaffected at 8 µg/ml. Albicidin targets DNA gyrase with features of inhibition that differ from those of other known antibiotics. It is synthesized by a unique hybrid polyketide synthase-nonribosomal peptide synthetase (PKS-NRPS) pathway that does not resemble any other pathway described to date. The antibiotic activity of albicidin against a wide range of gram-positive and gram-negative pathogenic bacteria (*Enterobacter aerogenes*, *E. coli*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Shigella sonnei*, and *Staphylococcus aureus*) is of interest for the development of new antibacterial drugs. Low yields of albicidin production in slow-growing *X. albilineans* have slowed studies of its chemical structure and potential therapeutic applications. Therefore, we have developed a heterologous system for albicidin overproduction using a *Xanthomonas axonopodis* pv. *vesicatoria* strain transformed with two plasmids harbouring the complete albicidin biosynthetic gene set. A sixty-fold increase in albicidin production was obtained when compared to albicidin production by the native host, *X. albilineans*. Heterologous production of albicidin was confirmed by FTICR-MS (high resolving Fournier Transform Ion Cyclotron Resonance Mass Spectrometry).